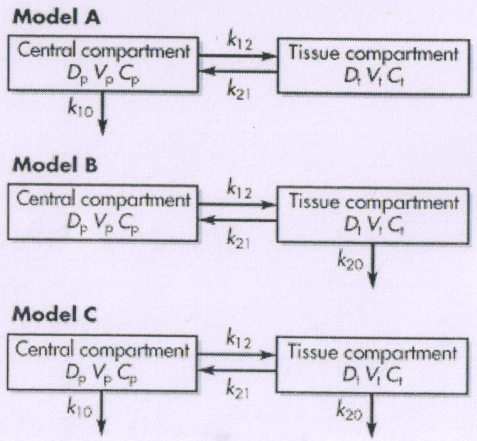
Two-compartment models

- There are several possible two-compartment models:

Two-compartment open models, intravenous injection



Two-compartment models

- Model A is used most often and describes the plasma level-time curve.
- By convention, compartment 1 is the central compartment and compartment 2 is the tissue compartment.

Two-compartment models

- The rate constants k_{12} and k_{21} represent the first-order rate transfer constants for the movement of drug from compartment 1 to compartment 2 (k_{12}) and from compartment 2 to compartment 1 (k_{21}).
- Most two-compartment models assume that elimination occurs from the central compartment model, as shown in (model A), unless other information about the drug is known.

Two-compartment models

- Drug elimination is presumed to occur from the central compartment, because the major sites of drug elimination (renal excretion and hepatic drug metabolism) occur in organs, such as the kidney and liver, which are highly perfused with blood.
- The plasma level-time curve for a drug that follows a two-compartment model may be divided into two parts, (i) a distribution phase and (ii) an elimination phase.

Two-compartment models

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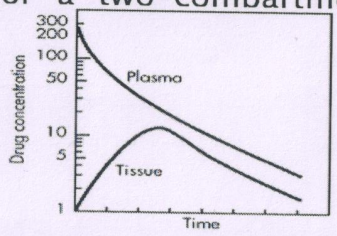
- After an IV bolus injection, drug equilibrates rapidly in the central compartment.
- The *distribution phase* of the curve represents the initial, more rapid decline of drug from the central compartment into the tissue compartment (line *a*).
- Although drug elimination and distribution occur *concurrently* during the distribution phase, there is a net transfer of drug from the central compartment to the tissue compartment.

Two-compartment models

(14)

- Relationship between tissue and plasma drug concentrations for a two-compartment open model.



- The maximum tissue drug concentration may be greater or less than the plasma drug concentration.

(15)

Two-compartment models

- The fraction of drug in the tissue compartment is now in equilibrium (*distribution equilibrium*) with the fraction of drug in the central compartment.
- The drug concentrations in both the central and tissue compartments decline in parallel and more slowly compared to the distribution phase. This decline is a first-order process and is called the *elimination phase* or the *beta* (β) phase (line *b*).
- At this point, drug kinetics appear to follow a one-compartment model in which drug elimination is a first-order process described by *b* (also known as beta).

(16)

Two-compartment models

- Tissue drug concentrations are theoretical only.
- The drug concentration in the tissue compartment represents the average drug concentration in a group of tissues rather than any real anatomic tissue drug concentration.
- In reality, drug concentrations may vary among different tissues and possibly within an individual tissue. These varying tissue drug concentrations are due to differences in the partitioning of drug into the tissues